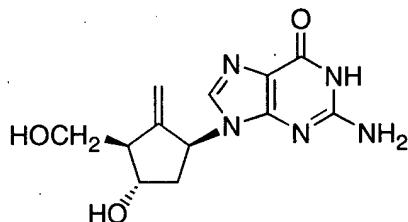


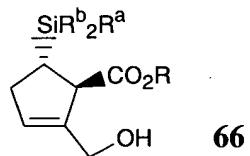
In the Claims:

1. (Currently amended) A process for the preparation of entecavir having the formula



21, comprising:

(a) treating an ester of the formula

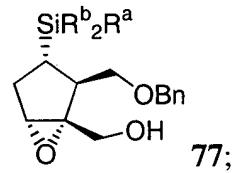


wherein R^a is allyl, phenyl, C_1 to C_6 alkylphenyl, or C_1 to C_6 alkoxyphenyl; R^b is C_1 to C_6 alkyl; and R is C_1 to C_4 alkyl or benzyl;

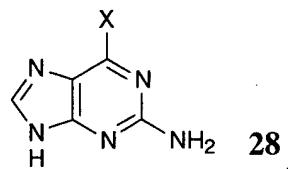
with an enol ether of acetone and an acid to protect the hydroxy group, followed by treatment with a hydride reagent to reduce the carboxylic acid ester moiety, and then alkylating the resulting alcohol with a benzyl halide and removing the enol ether hydroxy protecting group to give an allylic alcohol of the formula



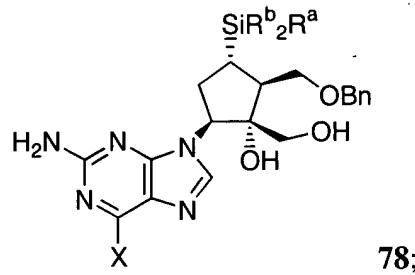
(b) epoxidizing the product from step (a) with a diastereoselective epoxidation to give a cyclopentane epoxide having the formula



(c) treating the cyclopentane epoxide from step (b) with an alkali metal salt of a purine compound of formula

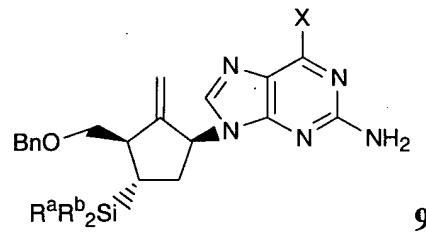


wherein X is Cl, I, or benzyloxy, to give a compound of formula



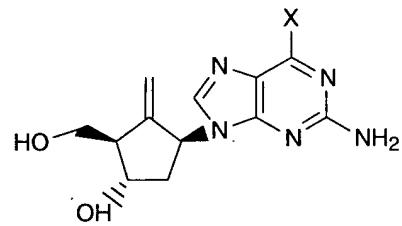
78;

(d) when X is Cl or I, converting eliminating the vicinal diol of formula 78 to form the methylene compound of formula,



94;

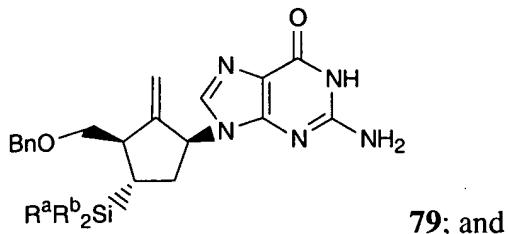
(e) hydrolyzing the benzyl ether moiety on the primary alcohol of compound 94 and converting transforming the silane moiety of compound 95 94 to a hydroxy moiety via protodesilylation and oxidation, to give a compound of formula,



95; and

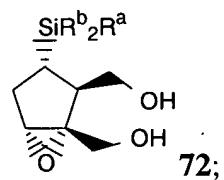
(f) hydrolyzing the chloro or iodo moiety X to provide the compound of formula 21; or

(d') when X is benzyloxy, converting eliminating the vicinal diol of formula 78 to form the methylene compound of formula

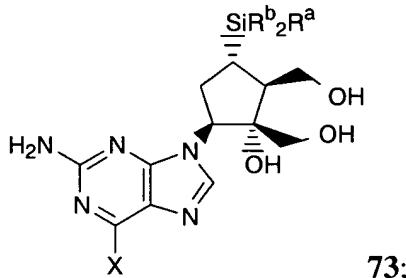


(e') hydrolyzing the benzyl ether moiety on the primary alcohol of compound 79 and converting transforming the silane moiety to a hydroxy moiety via protodesilylation and oxidation, to provide the compound of formula 21; or

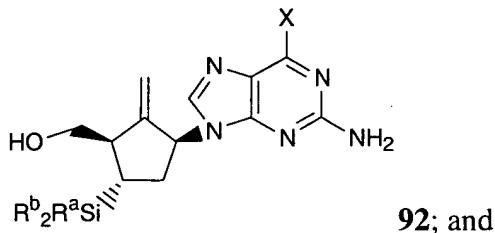
(a'') epoxidizing the ester of formula 66 with a diastereoselective epoxidation followed by reduction, to give a cyclopentane epoxide having the formula



(b'') treating the cyclopentane epoxide from step (a'') with an alkali metal salt of the purine compound of formula 28 to give a compound of formula

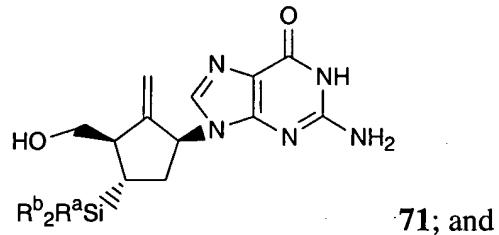


(c'') when X is Cl or I, converting eliminating the vicinal diol of formula 73 to form the methylene compound of formula



(d'') converting transforming the silane moiety of compound 92 to a hydroxy moiety via protodesilylation and oxidation, and hydrolyzing the chloro or iodo moiety X to provide the compound of formula 21; or

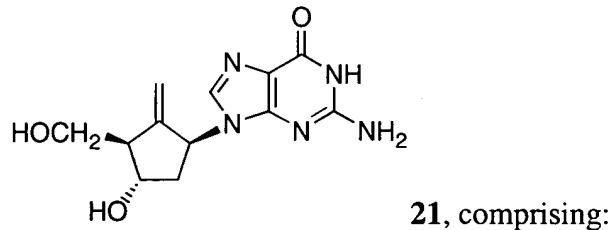
(c'') when X is benzyloxy, converting eliminating the vicinal diol of formula 73 to form the methylene compound of formula 71



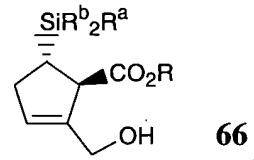
(d'') converting transforming the silane moiety of compound 71 to a hydroxy moiety via protodesilylation and oxidation, to provide the compound of formula 21.

2. (Original) The process of Claim 1, in which, in steps (b) and (a''), the diastereoselective epoxidation is performed with a peracid or with a homochiral diester of tartaric acid, a hydroperoxide, and a metal catalyst.

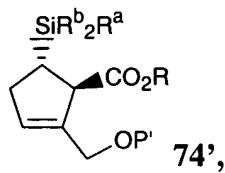
3. (Currently amended) A process for the preparation of entecavir having the formula



(a) protecting the hydroxy moiety of an ester of the formula

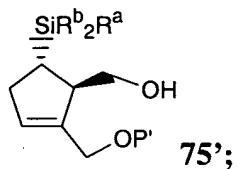


wherein R^a is allyl, phenyl, C₁ to C₆ alkylphenyl, or C₁ to C₆ alkoxyphenyl; R^b is C₁ to C₆ alkyl; and R is C₁ to C₄ alkyl or benzyl, to provide a compound of formula

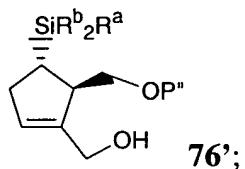


wherein P' is a protecting group;

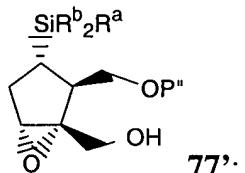
(b) reducing the carboxylic ester moiety of the compound 74' with at least one reducing reagent to provide a compound of formula,



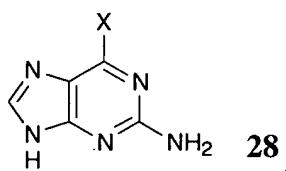
(c) protecting the unprotected hydroxy moiety of compound 75', with a protecting group P'' that is resistant to conditions used to remove P', then removing the protecting group P' of the compound of 75', to provide the compound having the formula,



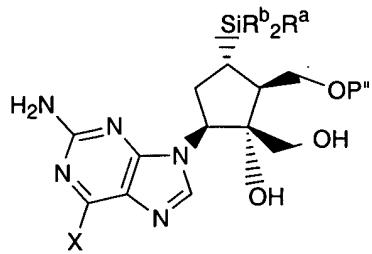
(d) epoxidizing the product from step (c) with a diastereoselective epoxidation to give a cyclopentane epoxide having the formula



(e) treating the cyclopentane epoxide from step (d) with an alkali metal salt of a purine compound of formula

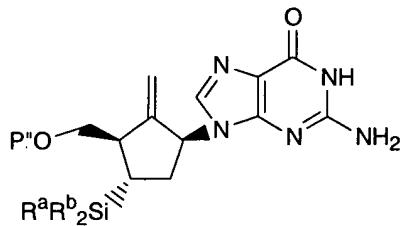


wherein X is Cl, I, or benzyloxy; to give a compound of formula



78'; then

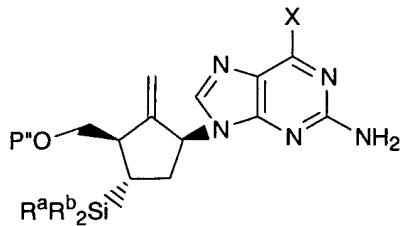
(f) when X is benzyloxy, converting eliminating the vicinal diol of formula 78' to provide the methylene compound of formula



79'; and

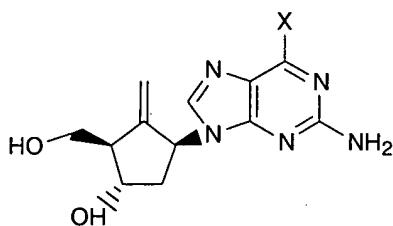
(g) removing the protecting group P'' on the primary alcohol of compound 79 and converting transforming the silane moiety to a hydroxy moiety via protodesilylation and oxidation, to provide the compound of formula 21; or

(f') when X is Cl or I, converting eliminating the vicinal diol of formula 78' to provide the methylene compound of formula,



94';

(g') removing the protecting group P'' on the primary alcohol of compound 94' and converting transforming the silane moiety to a hydroxy group via protodesilylation and oxidation, to give a compound of formula,



95; and

(h') hydrolyzing the chloro or iodo moiety X to provide the compound of formula 21.

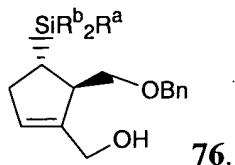
4. (Currently amended) The process of Claim 3, wherein, in step (g), the protecting group P" on the primary alcohol of compound 79' is benzyl, ~~said step of converting the silane moiety of compound 79 to a hydroxy group is achieved with protodesilylation and oxidation~~, and said benzyl protecting group is removed upon protodesilylation.

5. (Currently amended) The process of Claim 3, wherein the protecting group P" on the primary alcohol of compound 79' is removed after the silane moiety is ~~converted~~ transformed to a hydroxy moiety.

6. (Currently amended) The process of Claim 3, wherein in step (a), the hydroxy moiety is protected as a MOP by treatment with 2-methoxypropene and a catalytic amount of ~~a weak~~ an acid.

7. (Original) The process of Claim 3, wherein in step (b), the carboxylic ester moiety of the compound 74' is reduced with a hydride reagent selected from at least one of sodium bis(2-methoxyethoxy)aluminum hydride and lithium aluminum hydride in the presence of a base.

8. (Original) The process of Claim 3, wherein in step (c), the unprotected hydroxy moiety is protected as a benzyl ether upon treatment with a base and a benzyl halide, wherein, removal of the protecting group P' of the compound of 75' provides the allylic alcohol having the formula,



9. (Original) The process of Claim 8, wherein the base is selected from at least one of potassium *tert*-butoxide, sodium hydride, KHMDS, and aqueous NaOH, and the benzyl halide is benzyl bromide or benzyl chloride.

10. (Original) The process of Claim 3, in which in step (d), the diastereoselective epoxidation is performed by treatment with a peracid.

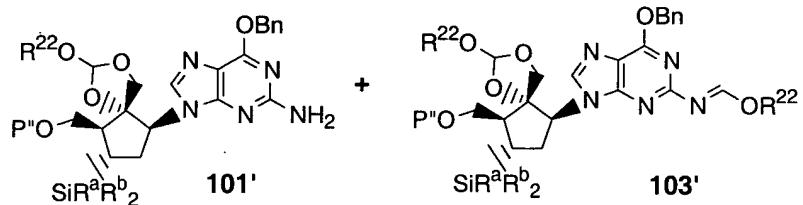
11. (Currently Amended) The process of Claim 3, in which in step (d), the diastereoselective epoxidation is performed by treatment with a homochiral diester of tartaric acid, a hydroperoxide, and a metal catalyst.

12. (Original) The process of Claim 11, wherein the homochiral diester of tartaric acid is (-)-diisopropyl tartrate, the hydroperoxide is *tert*-butylhydroperoxide or α,α -dimethylbenzylhydroperoxide, and the metal catalyst is titanium (IV) isopropoxide.

13. (Original) The process of Claim 3, wherein in step (e), the cyclopentane epoxide from step (d) is treated with 2-amino-6-benzyloxypurine in dichloromethane.

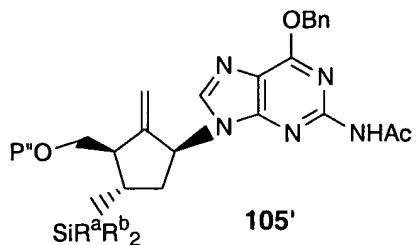
14. (Currently Amended) The process of Claim 3, wherein X is benzyloxy and in step (f), the elimination of the vicinal diol of compound 78' is converted to the methylene compound of formula **79'** is achieved by

(f)(i) treating compound **78'** with an orthoformate derivative in an inert solvent to produce a diastereomixture of dioxolanes having the formulae **101'** and **103'**,



wherein R²² is C₁₋₄alkyl or -C(=O)C₁₋₄alkyl;

(f)(ii) treating the product from step (f)(i) with an acetic anhydride in the presence of at least one antioxidant to produce an alkene compound having the formula **105'**;



; and

(f) (iii) treating the product from step (f)(ii) with an acid to hydrolyze the 6-benzyloxy and N-acetyl groups to provide the compound of formula 79'.

15. (Original) The process of Claim 14, wherein in step (f)(i), the orthoformate derivative is selected from at least one of diethoxymethyl acetate, diisopropoxymethyl acetate, TMOF, TEOF, and TiPOF.

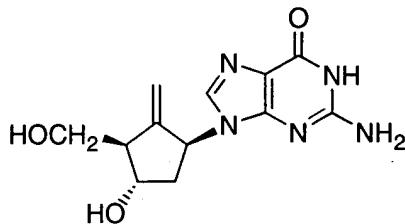
16. (Original) The process of Claim 14, wherein in step (f)(ii), at least one antioxidant is selected from BHT and benzoic acid.

17. (Currently amended) The process of Claim 3, ~~in which the step of converting the compound 79' to compound 21 is achieved with protodesilylation and oxidation, wherein in step (g) the protodesilylation is performed with KOH or NaOH in solvent, or with TFA, and the primary alcohol moiety is deprotected after the silane moiety is converted transformed to a hydroxy group, to provide the compound of formula 21.~~

18. (Currently amended) The process of Claim 3, ~~in which the step of converting the compound 79' to compound 21 is achieved with protodesilylation and oxidation, wherein the in step (g) of the protodesilylation is achieved with at least one acid selected from boron trifluoride-acetic acid complex and a Bronsted acid.~~

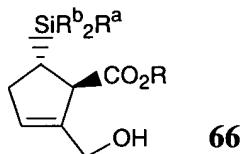
19. (Currently amended) The process of Claim 3, ~~in which the step of converting the compound 79' to compound 21 is achieved with protodesilylation and oxidation, and the wherein in step (g) the oxidation is achieved with hydrogen peroxide in the presence of potassium bicarbonate and optionally potassium fluoride.~~

20. (Currently Amended) A process for the preparation of entecavir having the formula

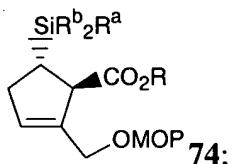


21, comprising:

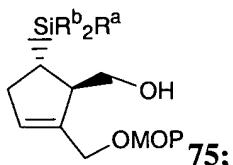
(a) treating an ester of the formula



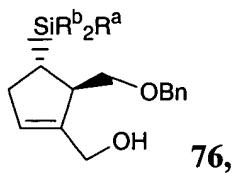
wherein R^a is allyl, phenyl, C₁ to C₆ alkylphenyl, or C₁ to C₆ alkoxyphenyl; R^b is C₁ to C₆ alkyl; and R is C₁ to C₄ alkyl or benzyl; with 2-methoxypropene and a catalytic amount of ~~a weak an~~ acid to provide a compound of formula



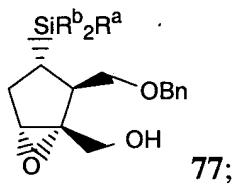
(b) reducing the carboxylic ester moiety of the compound **74** with a hydride reagent selected from at least one of sodium bis(2-methoxyethoxy)aluminum hydride and lithium aluminum hydride, in the presence of a base to provide a compound of formula,



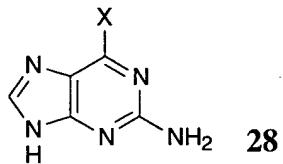
(c) protecting the unprotected hydroxy moiety of compound **75**, as a benzyl ether upon treatment of compound **75** with a base and a benzyl halide, then removing the MOP group of the compound **75**, to provide the allylic alcohol having the formula,



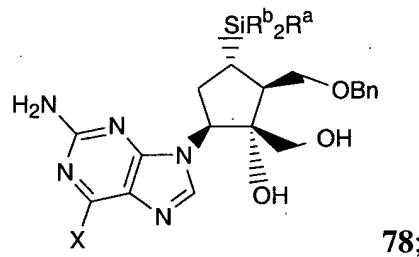
(d) epoxidizing the product from step (c) with (-)-diisopropyl tartrate, *tert*-butylhydroperoxide or cumene hydroperoxide, and titanium (IV) isopropoxide, to give a cyclopentane epoxide having the formula



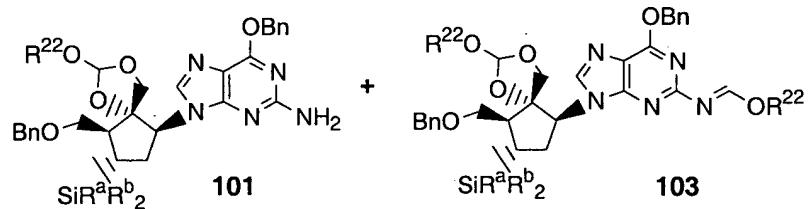
(e) treating the cyclopentane epoxide from step (d) with an alkali metal salt of a purine compound of formula



wherein X is benzyloxy; to give a compound of formula

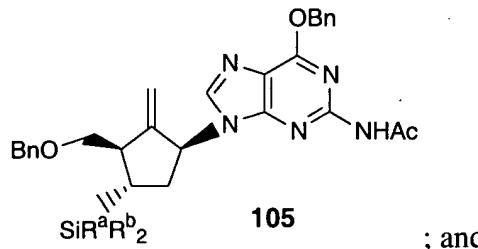


(f)(i) treating compound **78** with an orthoformate derivative selected from diethoxymethyl acetate and diisopropoxymethyl acetate in an inert solvent to produce a diastereomixture of dioxolanes having the formulae **101** and **103**,



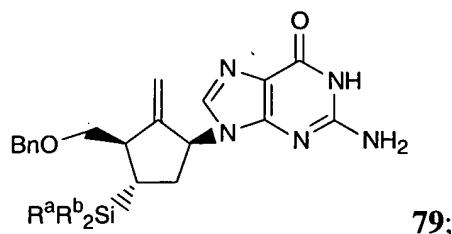
wherein R²² is ethyl, -C(=O)ethyl, isopropyl, or -C(=O)isopropyl;

(f)(ii) treating the product from step (f)(i) with an acetic anhydride in the presence of BHT to produce an alkene compound having the formula 105;



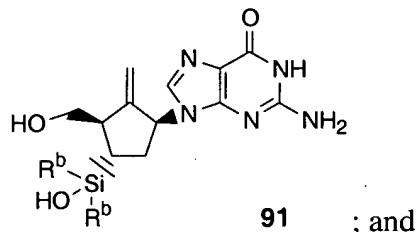
; and

(f) (iii) treating the product from step (f)(ii) with an acid to hydrolyze the 6-benzyloxy and N-acetyl groups and provide the compound of formula 79,



(g) converting transforming the silane moiety to a hydroxy moiety by protodesilylating the silane moiety of compound 79 upon treatment with at least one reagent effective to achieve protodesilylation, followed by oxidation with a peroxide, and debenzylating compound 79, wherein debenzylation may be achieved upon protodesilylation, to provide the compound of formula 21.

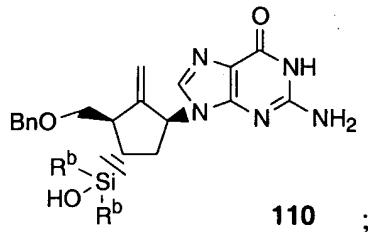
21. (Original) The process of Claim 20, in which step (g) comprises treating compound 79 with an acid selected from boron trifluoride-acetic acid complex and a Bronsted acid, wherein said step of protodesilylation removes the benzyl protecting group of compound 79 to provide the compound of formula 91,



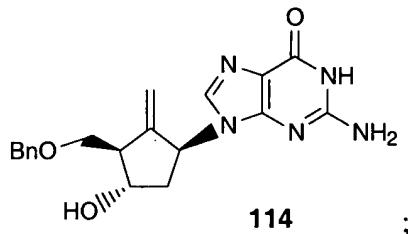
; and

oxidizing the compound **91** with hydrogen peroxide in the presence of potassium bicarbonate and potassium fluoride to provide the compound **21**.

22. (Original) The process of Claim 20, in which step (g) comprises treating compound **79** with potassium hydroxide or sodium hydroxide in solvent, or TFA to provide the compound of formula **110**,



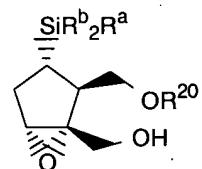
oxidizing compound **110** with hydrogen peroxide in the presence of potassium bicarbonate and potassium fluoride to provide the compound **114**;



and debenzylating compound **114** to provide compound **21**.

23-40. (Withdrawn)

41. (Original) A compound of formula



wherein:

R^a is alkyl, phenyl, C₁ to C₆ alkylphenyl, or C₁ to C₆ alkoxyphenyl;

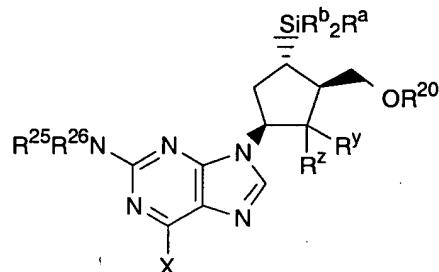
R^b is C₁ to C₆ alkyl; and

R²⁰ is hydrogen or benzyl.

42. (Original) The compound of Claim 41 wherein:

R^a is phenyl;
 R^b is methyl; and
 R^{20} is benzyl.

43. (Original) A compound of formula



or a salt thereof wherein:

R^a is alkyl, phenyl, C_1 to C_6 alkylphenyl, or C_1 to C_6 alkoxyphenyl;
 R^b is C_1 to C_6 alkyl;
 R^{20} is hydrogen or benzyl;
 X is Cl, I, or benzyloxy;
 R^y and R^z are taken together to form methylene ($=CH_2$), or R^y is OR^{23} , and R^z is $-CH_2OR^{24}$, wherein R^{23} and R^{24} are each hydrogen or are taken together to form a ring to define a dioxolane, said dioxolane being optionally substituted with $-O(C_{1-4}\text{alkyl})$ or $-O(C=O)(C_{1-4}\text{alkyl})$; and
 R^{25} and R^{26} are both hydrogen, or one of R^{25} and R^{26} is hydrogen and the other is acyl; or R^{25} and R^{26} are taken together to form $=CH(OC_{1-4}\text{alkyl})$ or $=CH(OC(=O)C_{1-4}\text{alkyl})$.

44. (Original) The compound of Claim 43 wherein:

R^a is phenyl;
 R^b is methyl; and
 X is benzyloxy.

45. (Original) The compound of claim 44 in which

R^{20} is benzyl;
 R^y is OH, and R^z is $-CH_2OH$, and

R^{25} and R^{26} are both hydrogen.

46. (Original) The compound of Claim 43 wherein:

R^a is phenyl;

R^b is methyl;

X is benzyloxy;

R^y is OR^{23} , and R^z is $-CH_2OR^{24}$, wherein R^{23} and R^{24} combine to form a dioxolane optionally substituted with $-O(C_{1-4}\text{alkyl})$ or $O(C=O)(C_{1-4}\text{alkyl})$; and
 R^{25} and R^{26} are both hydrogen, or R^{25} and R^{26} are taken together to form
 $=CH(OC_{1-4}\text{alkyl})$ or $=CH(O(C=O)C_{1-4}\text{alkyl})$.

47. (Original) The compound of Claim 43 wherein:

R^a is phenyl;

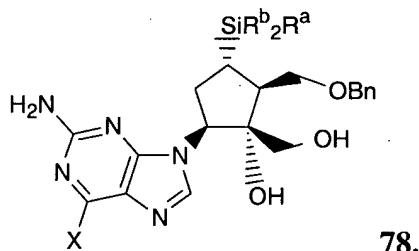
R^b is methyl;

X is benzyloxy;

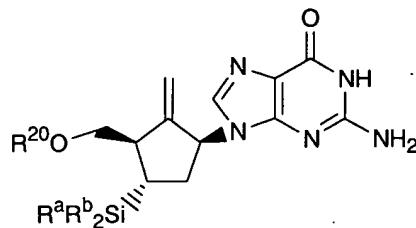
R^y and R^z are taken together to form methylene; and

R^{25} is hydrogen and R^{26} is acyl.

48. (Original) The compound of Claim 43 having the formula,



49. (Original) A compound of formula



or a salt thereof, wherein:

R^a is alkyl, phenyl, C₁ to C₆ alkylphenyl, or C₁ to C₆ alkoxyphenyl;

R^b is C₁ to C₆ alkyl; and

R²⁰ is hydrogen or benzyl.

50. (Original) The compound of Claim 49 wherein:

R^a is phenyl;

R^b is methyl; and

R²⁰ is hydrogen.

51. (Original) The compound of Claim 49 wherein:

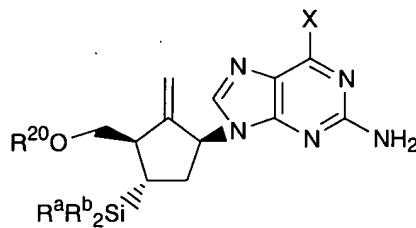
R^a is phenyl;

R^b is methyl; and

R²⁰ is benzyl.

52. (Original) The methanesulfonate salt of the compound of Claim 51.

53. (Original) A compound of formula



or a salt thereof, wherein:

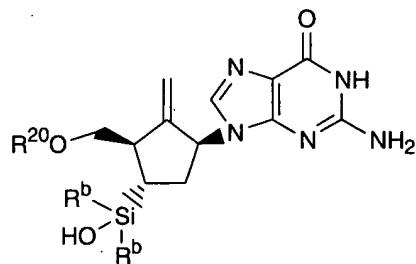
X is Cl or I;

R^a is alkyl, phenyl, C₁ to C₆ alkylphenyl, or C₁ to C₆ alkoxyphenyl;

R^b is C₁ to C₆ alkyl; and

R²⁰ is hydrogen or benzyl.

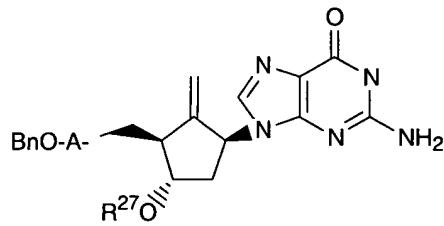
54. (Original) A compound of formula



wherein R^b is C_1 to C_6 alkyl; and R^{20} is hydrogen or benzyl, or a salt thereof.

55. (Original) The compound of Claim 54 wherein R^b is methyl.

56. (Original) A compound of formula



or a salt thereof, wherein:

A is CH_2 or a bond;

R^{27} is hydrogen, benzyl, or $SiR^d_2R^c$;

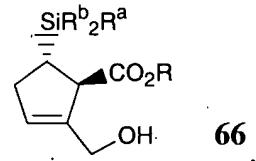
R^c is C_1 to C_4 alkyl or phenyl; and

R^d is C_1 to C_3 alkyl.

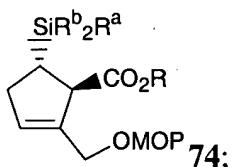
57. (Original) A compound of claim 56, in which A is a bond, and R^{27} is hydrogen.

58. (Original) A method for making a compound of formula 78, according to Claim 48, comprising,

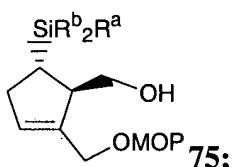
(a) treating an ester of the formula



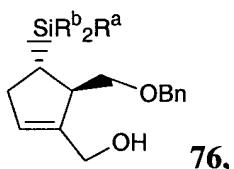
wherein R^a is allyl, phenyl, C_1 to C_6 alkylphenyl, or C_1 to C_6 alkoxyphenyl; R^b is C_1 to C_6 alkyl; and R is C_1 to C_4 alkyl or benzyl; with 2-methoxypropene and a catalytic amount of a weak an acid to provide a compound of formula



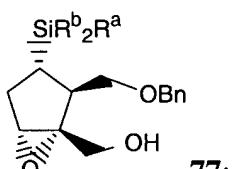
(b) reducing the carboxylic ester moiety of the compound 74 with at least one hydride reagent to provide a compound of formula,



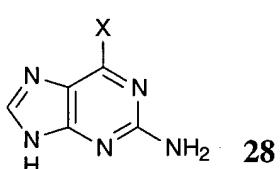
(c) protecting the unprotected hydroxy moiety of compound 75, as a benzyl ether upon treatment of compound 75 with a base and a benzyl halide, then removing the MOP group of the compound 75, to provide the allylic alcohol having the formula,



(d) epoxidizing the product from step (c) with a diastereoselective epoxidation, to give a cyclopentane epoxide having the formula



(e) treating the cyclopentane epoxide from step (d) with an alkali metal salt of a purine compound of formula



wherein X is benzyloxy; I, or Cl, to give a compound of formula **78**.

59-74. (Withdrawn)